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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,336	10/29/2002	Susumu Suzuki	082375-000000US	9875

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EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 12/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,336	SUZUKI ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-2 and 5-15, drawn to a method of measuring a kinase activity of a cyclin/CDK complex on RB proteins and a method of screening for compounds that inhibit or inhance such kinase activity.

Group II, claim(s) 3, 5-8, and 10-15, drawn to a method of measuring a phosphatase activity on phosphorylated RB proteins.

Group III, claim(s) 4-8 and 10-15, drawn to a method of screening for compounds that inhibit or enhance phosphatase activity on phosphorylated RB proteins.

Group IV, claim(s) 16 and 18, drawn to a protein kinase activity regulating agent of a cyclin/CDK complex.

Group V, claim(s) 17-18, drawn to a phosphatase activity regulating agent of a protein.

Group VI, claim(s) 19-22, drawn to an immunogen for preparing antibodies.

Group VII, claim(s) 23, drawn to a kit containing an antibody that identifies the phosphorylation state of the substrate.

2. The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups I-VII appears to be the feature of measuring a kinase or phosphatase activity with respect to a protein substrate that is phosphorylated by a cyclin/CDK complex, using antibodies that detect phosphorylated forms of the substrate.

However, Kitagawa et al. (EMBO **15**:7060-7069, 1996, Applicant's Information Disclosure Statement) teach a contacting a substrate (RB protein or synthetic peptides containing a part of the sequence of RB) with a cyclin/CDK complex (for example, cyclin A/CDK2 or Cyclin D1/CDK4) under conditions required for the phosphorylation reaction to occur (see in particular the abstract and Figure 1; p. 7061, "Results"; p. 7064-7065, "Phosphorylation of Ser780 in pRB in vitro and in vivo"; and p. 7069, "In vitro kinase assay"). Kitagawa et al. further teach detecting changes in the phosphorylation level of an RB protein substrate with antibodies that identify the phosphorylation state of the substrate (see p. 7068, "Antibodies").

Therefore, the technical feature linking the inventions of Groups I-VII does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

In addition, Groups I-VII each have technical features that are unrelated to the other groups. Group I has the technical feature of selecting a compound that lowers or elevates the phosphorylation level of the substrate, which is not a feature of Groups II-VII. Group II includes the feature of incubating a phosphorylated RB protein substrate that is phosphorylated by a cyclin/CDK complex under conditions required for a dephosphorylation reaction to occur, which is not a feature of Groups I or III-VIII. Group III includes the feature of incubating a phosphatase with a substrate in the presence of a test compound, which is not a feature of Groups I-II or IV-VIII. Group IV includes the feature of a protein kinase activity regulating agent containing a

compound; Group V includes the feature of a protein phosphatase activity regulating agent; Group VI includes the feature of an immunogen for preparing antibodies; and Group VII includes the feature of a kit containing an antibody that identifies the phosphorylation state of a substrate, which are not features of the other groups.

Accordingly, Groups I-VII are not linked by the same or a corresponding special technical feature so as to form a single general inventive concept.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

In the event that Groups I, II, III, or IV are elected, the following species elections must also be made (for both (a) and (b)):

a. A single type of cyclin (elect one of the following):

i. Cyclin A

ii. Cyclin B

iii. Cyclin D1

iv. Cyclin D2

v. Cyclin D3

vi. Cyclin E

b. A single type of CDK (elect one of the following):

i. CDK1

ii. CDK2

iii. CDK4

iv. CDK6

Currently, claims 1-4, 9, 10-16 and 18 are generic. Claims 5-8 are subject to species election.

In the event that Group V is elected, the following species election must also be made:

a. One protein that is phosphorylated by the kinase of a cyclin/CDK complex

An election of a protein that is phosphorylated by the kinase of a cyclin/CDK complex may be specified by identifying a single protein, either by name or by SEQ ID NO.

In the event that Group VI is elected, the following species election must also be made:

a. One RB protein or peptide comprising an amino acid sequence including one or more phosphorylation sites of the homologues of the RB protein (elect one of the following):

i. The RB protein

ii. SEQ ID NO:2

iii. SEQ ID NO:4

iv. SEQ ID NO:6

v. SEQ ID NO:8

Should Applicant wish to elect an RB protein or peptide that is not listed above, this may be done by identifying a single protein or peptide by name or by SEQ ID NO.

Currently, claim 19 is generic. Claims 20-22 are subject to species election.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

2. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

These species of cyclin and CDK polypeptides are distinct in that the species are each unique molecules, bearing distinct amino acid sequences, such that they possess different chemical and structural features. The various cyclin/CDK complexes formed from the different species of cyclin and CDK species also differ with respect to activity and substrate specificity (see the specification, for example at p. 35, lines 16-18). For example, the Cyclin A/CDK2

complex has selectivity to a certain amino acid residue on the substrate, while the Cyclin D/CDK4 complex lacks this technical feature in that it is selective towards a different amino acid residue. Moreover, the different reactivities of the various combinations of cyclin/CDKs would require that the methods of Groups I-III employ different reagents (antibodies) to detect and identify the phosphorylated RB protein substrates. These different antibodies required to detect and identify the phosphorylated substrates are disclosed, for example, at p. 33, lines 20-23. With respect to Group IV, since the different cyclin/CDK complexes have different activities, an agent that regulates the activity of one complex would not necessarily regulate the activity of other complexes.

The species of proteins that are phosphorylated by the kinase of a cyclin/CDK complex, as recited in claim 17, lack the same or corresponding special technical feature in that the different cyclin/CDK complexes have different reactivities, as discussed above, such that proteins phosphorylated by one complex would not necessarily have the same pattern or number of phosphorylations as the proteins phosphorylated by a different complex. As a result, agents that regulated the phosphatase activity of one protein would not necessarily regulate the activity of a different protein having a different number or type of phosphorylated residues.

The species of RB protein or peptide comprising an amino acid sequence including one or more phosphorylation sites of the homologues of the RB protein lack the same or corresponding special technical feature in that they bear distinct amino acid sequences and therefore chemical and structural features, as well as different phosphorylation patterns leading to different substrate activities and different selectivities for kinases and phosphatases.

A telephone call was made to Joe Liebeschuetz on November 30, 2005 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Notice of Possible Rejoinder

The Examiner notes that the instant application is a national stage entry of PCT/JP00/05219 filed under 35 U.S.C. § 371. For purposes of restriction, lack of unity practice has been applied to the pending claims under 35 U.S.C. § 121 and 372. Lack of unity will be reassessed at each stage of prosecution hereafter.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter

of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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12/06/05